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SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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REF: EXPEDIENTE 04-117-654

TÍTULO SOLICITADO: "Compuestos derivados sustituidos de Sulfamato de fórmula (I) útiles como anticonvulsivos para el tratamiento de la epilepsia, procedimiento para su preparación y composición farmacéutica que lo comprende"

PUBLICACIÓN: Gaceta 562 de 31-03-2006, número de publicación 1311

PRIORIDAD : US 60/378,017 de mayo 13 de 2002

SOLICITANTE: ORTHO-MCNEIL PHARMACEUTICAL, INC

APODERADO: JIMENA ESCOBAR URIBE

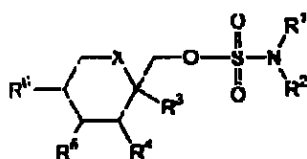
TRÁMITE: SUSTENTACIÓN DE OPOSICIÓN

JOSÉ LUIS REYES VILLAMIZAR, identificado como aparece al pie de mi firma, reconocido apoderado del opositor en el trámite de la referencia, estando dentro de los términos de la prórroga solicitada, por medio del presente escrito me permito ratificar y sustentar los argumentos del escrito principal de oposición, también radicado dentro del plazo de ley ante esa entidad.

I. RATIFICACIÓN

Reitero a su Despacho la solicitud de negar el beneficio patentario para la totalidad de las reivindicaciones contenidas en el expediente en referencia, por los argumentos expuestos en el escrito de oposición presentado en 04/07/2006.

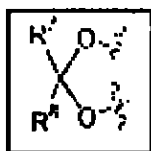
Lo anterior, en tanto es evidente que el compuesto de fórmula (I) o una sal farmacéuticamente aceptable del mismo, una composición farmacéutica que lo contiene junto con un vehículo adecuado, el método de tratamiento y el proceso de obtención revelados en la solicitud colombiana 04-117-654 en trámite **carecen de nivel inventivo**. En efecto, el compuesto de fórmula (I)



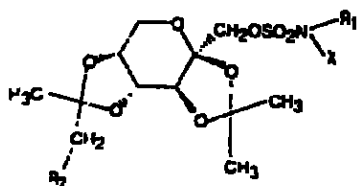
(I)

con sus respectivos sustituyentes X= CH₂ u O;

Cuando X es O, R₃ y R₄ y/o R₅ y R₆ juntos pueden ser un grupo metilendioxi de la



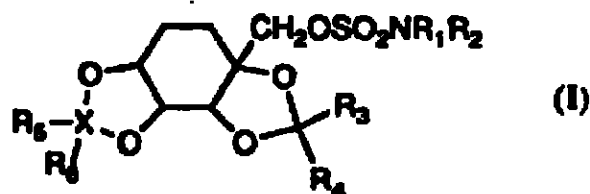
fórmula es muy similar a los compuestos revelados en la publicación internacional WO97/19950 titulada "Topiramate Immunoassay, as well as analogs and antibodies", ya que se describen análogos de Topiramato de la siguiente fórmula:



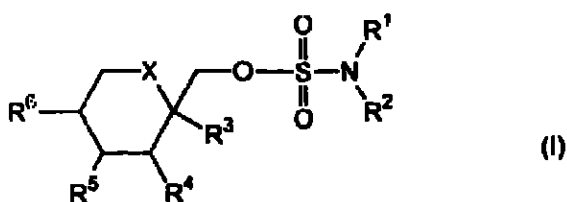
Tanto en el compuesto revelado en las reivindicaciones 1 y 2 de la solicitud colombiana como en el descrito en la página 3 de la citada publicación internacional, los compuestos en una y otra son prácticamente idénticos puesto que ambos contienen en su estructura la presencia de dos grupos metilendioxi, un grupo D-fructopiranos, y una cadena de tipo sulfamato siendo la única diferencia el radical R₁ señalado en color naranja, ya que no coinciden en el tipo de sustituyente.

De igual manera, la reivindicación 24 de la solicitud que nos ocupa, en tanto los compuestos mencionados en ésta son derivados o análogos de Topiramato, también se encuentran anticipados en la solicitud internacional WO 97/19950 puesto que se refiere a compuestos derivatizados o análogos de Topiramato por lo tanto, le resta por completo nivel inventivo a los compuestos de la solicitud colombiana en trámite.

Por su parte, la solicitud internacional WO 95/17406 publicada en junio de 1995, revela compuestos de fórmula (I) los cuales son potentes fármacos



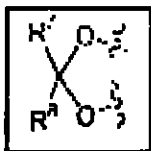
anticonvulsivantes y que son muy similares a los compuestos de fórmula (I) de la solicitud colombiana



con sus respectivos sustituyentes X=

CH₂ u O;

Cuando X es O, R₃ y R₄ y/o R₅ y R₆ juntos pueden ser un grupo metilendioxi de la



fórmula puesto que uno y otro contienen en su estructura la presencia de dos grupos metilendioxi y una cadena de tipo sulfamato siendo la única diferencia la ausencia de un grupo O señalado en color rojo en los compuestos de la solicitud WO 97/17406, por lo que se designan en dichos documentos como Pseudofructopiranos sulfamatos.

II. COMPLEMENTO DE INFORMACIÓN

En adición a lo expuesto en el punto precedente y en el escrito inicial de oposición, ruego al Despacho se sirva tener en cuenta los siguientes argumentos:

La patente europea EP 0 138 441 "ANTICONVULSIVANT SULFAMATE DERIVATIVES" publicada el 24 de abril de 1985 y con prioridad US 53475 de 25-09-1984, revela sulfamatos de fórmula (I) que exhiben actividad anticonvulsivante y son usadas en el tratamiento de condiciones tales como epilepsia, también describe composiciones farmacéuticas que contienen compuestos de fórmula (I) así como métodos para su uso e intermediarios.

Resulta interesante establecer una comparación detallada entre dicha patente y la solicitud colombiana en trámite, así:

EP 0 138 441 (24-04-1985)	Solicitud Colombiana 04-117-654
Rv 1: Sulfamatos de la siguiente formula (I): en donde: X= O ó CH₂; R1= H o alquilo; R2, R3, R4 y R5= H, alquilo inferior. Cuando X es O, R₂ y R₃ y/o R₄ y R₅ juntos pueden ser un grupo metilendioxi de la fórmula	Rv 1: Un compuesto de fórmula (I) en donde: X= CH₂ u O; R1= H, alquilo, alquenilo, alquinilo, cicloalquilo... entre otros R2= Hidroxi, alquilo, alcoxi, alquenilo, alquinilo, cicloalquilo... entre otros Cuando X es O, R₃ y R₄ y/o R₅ y R₆ juntos pueden ser un grupo metilendioxi de la fórmula
Luego de algunas sustituciones tenemos: R1= H o <u>alquilo</u>	Rv 2: El compuesto de conformidad con la reivindicación 1, caracterizado además porque es de fórmula (It) Donde R1= <u>H</u>, alquilo, alquenilo, alquinilo, cicloalquilo... entre otros R2= Hidroxi, <u>alquilo</u>, alcoxi, alquenilo, alquinilo, cicloalquilo... entre otros

EP 0 138 441 (24-04-1985)	Solicitud Colombiana 04-117-654
Rv 9: Una composición farmacéutica que comprende un sulfamato de cualquiera de las reivindicaciones precedentes y un vehículo farmacéuticamente aceptable.	Rv 14: Una composición farmacéutica que comprende un portador farmacéuticamente aceptable y un compuesto de la reivindicación 1.
Rv 13: Un método para fabricar un sulfamato de acuerdo con la reivindicación 1. Rv 6 y 7: El sulfamato de fórmula (I) es seleccionado del grupo de varios compuestos, entre los que se encuentra: 2,3:4,5-bis-O(1-methylethylidene)-β-D-fructopyranose sulfamate (Topiramato)	Rv 23: Un procedimiento para la preparación de un compuesto de fórmula XXa (que corresponde a Topiramato)

Una simple observación de los esquemas anteriores permite concluir que, tanto los sulfamatos de fórmula (I) de la EP 0 138 441 como el compuesto de fórmula (I) de la solicitud colombiana en trámite y teniendo en cuenta por supuesto las sustituciones pertinentes son "idénticos" puesto que ambos contienen en su estructura la presencia de dos grupos metilendioxi, un grupo D-fructopiranososa, una cadena de tipo sulfamato, y el Nitrógeno se encuentra sustituido por un radical H y por un radical alquilo.

De igual manera, es importante resaltar que, la publicación europea también revela un método de obtención de estos sulfamatos que si bien es cierto no es igual al revelado en la solicitud colombiana, no lo es menos que por ambos métodos pueden obtenerse sustancias como "Topiramato"

Lo expuesto supone que la existencia de los compuestos revelados en la publicación europea EP 0 138 441 le resta por completo nivel inventivo a los compuestos de la solicitud colombiana en trámite, en tanto unos y otros son derivados sustituidos de sulfamatos y estructuralmente son "idénticos", además, que describe un método que permite obtener "topiramato", entre otros compuestos.

III. PRUEBAS

Ruego que se tenga como tal, sin perjuicio de que el Despacho considere oficiosamente y de las ya aportadas por el suscrito, la siguiente:

- Publicación europea EP 0 138 441 de junio abril 24 de 1985, páginas 1 a 1

Señor Superintendente,



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T.P.A. 44.655 del C.S.J.



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EUROPEAN PATENT APPLICATION

Application number: 8438512.9

Date of filing: 25.08.84

Int. Cl.⁴: C 07 C 143/08, C 07 D 309/08,
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⑤ Priority: 28.08.83 US 528475

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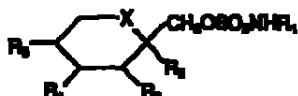
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⑪ Anticonvulsant carbonate derivatives.

⑫ Substances of the following formula (I):



wherein X is O or CH₂ and R₁, R₂, R₃, R₄ and R₅ are as herein
defined have been found to exhibit anticonvulsant activity and are
thus useful in the treatment of conditions such as epilepsy.
Further, pharmaceutical compositions containing a compound of
formula (I) as well as methods for their use and intermediates
form part of the present invention.

EP 0 138 441 A2

ANTICONVULSANT SULFAMATE DERIVATIVES

Sulfamates of various structures, including those derived from monosaccharides are described in references such as
5 N.K. Kochetkov et al in Zhurnal Obshchei Khimii, Vol. 41, No. 8, 1866 to 1871 (1971), Vol. 42, No. 12, 2755 to 2757 (1972) and Vol. 44, No. 4, 871 to 875 (1974) and in Doklady Akademii Nauk SSSR, Vol. 216, No. 1, 97 to 100 (1974); T. Tsuchiya et al., in Tetrahedron Letters,
10 No. 36, 3365 to 3368 (1978); and A.P. Hirsch in Journal of Medicinal Chemistry, 24, 901 to 903 (1981) and U.S. Patent 4,075,351.

15 Summary of the Invention

It has been found that sulfamates of the following formula (I):



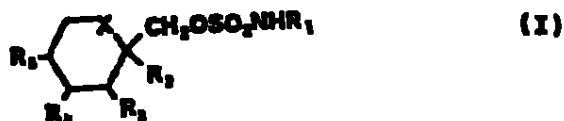
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wherein X is O or CH₂ and R₁, R₂, R₃, R₄ and R₅ are as hereinafter defined, possess anticonvulsant activity in mammals and are thus useful in treating disease states
25 such as epilepsy and glaucoma. Also part of the present invention are pharmaceutical compositions containing one or more sulfamates of formula (I) as well as methods for the treatment e.g., prevention, of convulsions using such compositions.

Detailed Description of the Invention

The sulfamates of the invention are of the following formula (I):

5



wherein

10

X is CH₂ or oxygen;

(e.g. C₁ to C₆ alkyl);

R₁ is hydrogen or alkyl/ and

15

R₂, R₃, R₄ and R₅ are independently hydrogen or lower alkyl (e.g. C₁ to C₄ alkyl), and, when X is CH₂, R₄ and R₅ may be joined to form a benzene ring and, when X is oxygen, R₂ and R₃ and/or R₄ and R₅ together may be a methylenedioxy group of the following formula (II):

20

(II)



wherein

25

R₆ and R₇ are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

R₁ is preferably hydrogen or alkyl of about 1 to 4 carbons, such as methyl, ethyl and iso-propyl. Alkyl throughout this specification includes straight and branched chain alkyl. Specific alkyl groups for R₂, R₃, R₄, R₅, R₆ and R₇ include methyl, ethyl, iso-propyl and n-propyl. When X is CH₂, R₄ and R₅ may combine to form a

benzene ring fused to the 6-membered X-containing ring, i.e., R_4 and R_5 are defined by the alkatrienyl group $-CH=CH=CH-$.

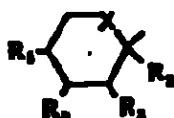
- 5 A particular group of compounds of formula (I) is that wherein X is oxygen and both R_2 and R_3 and R_4 and R_5 together are methylenedioxy groups of the formula (II) wherein R_6 and R_7 are both hydrogen, both alkyl or combine to form a spiro cyclopentyl or cyclohexyl ring, in
10 particular where R_6 and R_7 are both alkyl such as methyl. A second group of compounds is that wherein X is CH_2 and R_4 and R_5 are joined to form a benzene ring. A third group of compounds of formula (I) is that wherein both R_2 and R_3 are hydrogen.

15

The compounds of formula (I) may be synthesized by the following methods:

- a) Reaction of an alcohol of the formula RCH_2OH with a
20 chlorosulfonate of the formula $ClSO_2NH_2$ or $ClSO_2NHR_1$ in the presence of a base such as potassium t-butoxide or sodium hydride at a temperature of about -20 to $25^\circ C$ and in a solvent such as toluene, THF or dimethylformamide wherein R is a moiety of the following formula (III):

25



(III)

30

- b) Reaction of an alcohol of the formula RCH_2OH with
sulfurylchloride of the formula SO_2Cl_2 in the presence of
a base such as triethylamine or pyridine at a temperature
of about -40 to $25^\circ C$ in a solvent such as diethyl ether
35 or methylene chloride to produce a chlorosulfate of the
formula RCH_2OSO_2Cl .

The chlorosulfate of the formula RCH_2OSO_2Cl may then be reacted with an amine of the formula R_1NH_2 at a temperature of about -40 to $25^\circ C$ in a solvent such as methylene chloride or acetonitrile to produce a compound of formula (I). The reaction conditions for b) are also described by T. Tsuchiya et al in Tet. Letters, No. 36, p. 3365 to 3368 (1978).

c) Reaction of the chlorosulfate RCH_2OSO_2Cl with a metal azide such as sodium azide in a solvent such as methylene chloride or acetonitrile yields an azidosulfate of the formula $RCH_2OSO_2N_3$ as described by M. Nedayatullah in Tet. Lett. p. 2455-2458 (1975). The azidosulfate is then reduced to a compound of formula (I) wherein R_1 is hydrogen by catalytic hydrogenation, e.g. with a noble metal and H_2 or by heating with copper metal in a solvent such as methanol.

The starting materials of the formula RCH_2OH may be obtained commercially or as known in the art. For example, starting materials of the formula RCH_2OH wherein both R_2 and R_3 and R_4 and R_5 are identical and are of the formula (II) may be obtained by the method of R. F. Brady in Carbohydrate Research, Vol. 15, p. 35 to 40 (1970) or by reaction of the trimethylsilyl enol ether of a R_6COR , ketone or aldehyde with fructose at a temperature of about $25^\circ C$ in a solvent such as a halocarbon, e.g. methylene chloride in the presence of a protic acid such as hydrochloric acid or a Lewis Acid such as zinc chloride. The trimethylsilyl enol ether reaction is described by G. L. Larson et al in J. Org. Chem. Vol. 38, No. 22, p. 3935 (1973).

Further, carboxylic acids and aldehydes of the formulae $RCOOH$ and $RCHO$ may be reduced to compounds of the formula RCH_2OH by standard reduction techniques, e.g. reaction

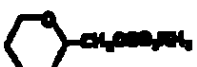
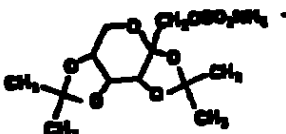
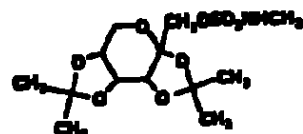
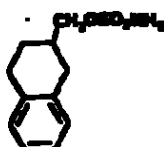
with lithium aluminum hydride, sodium borohydride or borane-THF complex in an inert solvent such as diglyme, THF or toluene at a temperature of about 0 to 100°C, e.g., as described by R. O. House in "Modern Synthetic Reactions", 2nd Ed., pages 45 to 144 (1972).

The compounds of the invention include the various individual isomers as well as the racemates thereof, e.g., the various alpha and beta attachments, i.e., below and above the plane of the drawing, of R₁, R₂, R₃ and R₄ on the 6-membered ring. Preferably, the oxygens of the methylenedioxy group (II) are attached on the same side of the 6-membered ring.

The compounds of formula (I) are useful as anticonvulsant agents. The anticonvulsant activity of the subject compounds was determined using a standard "maximal electroshock test" (MES). In this test, activity is indicated by a block of the tonic extensor seizure caused by application of an electric shock to mice via corneal electrodes, as described by Swinyard et al in J. Pharmacol. Exptl. Therap. 106, 319 (1952), and recorded as a block. A more recent description of current anticonvulsant drug screening is given in Swinyard et al in Epilepsia 19, 409 (1978).

The anticonvulsant activity of compounds of this invention tested according to the Swinyard (1952) method is shown in the following Table I:

TABLE I

Example	Compound	MES test ED ₅₀ * (mg/kg, i.p.)
5	1	195
		
10	2	270
		
15	3	26
		
20	4	70% block at 200 mg/kg, i.p.
		
25	5	55
		

* Unless otherwise noted.

35

For treating epilepsy, a compound of formula (I) may be employed at a daily dosage in the range of about 30 to

2000 mg, usually in 2 to 4 divided doses, for an average adult human. A unit dose would contain about 10 to 500 mg of the active ingredient.

- 5 In general, compounds of formula (I) may be used in treating epilepsy in a manner similar to that used for phenytoin. Medical aspects of the treatment of epilepsy are described by L.S. Goodman et al in "The Pharmacological Basis of Therapeutics", 5th Ed. pages 201 to 226,
10 Macmillan (1975).

- Further, compounds of formula (I) are inhibitors of carbonic anhydrase, as determined by the methods described by S. J. Dodgson et al in the Proc. Natl. Acad. Sci.,
15 U.S.A., 77, pages 5562 to 5566 (1980) or by H. Itada et al in the Journal Biol. Chem., 252, pages 3881 to 3890 (1977) and as such, are useful in the treatment of glaucoma. The relationship between the treatment of glaucoma and carbonic anhydrase inhibition is described by A. Stein et
20 al in the American Journal of Ophthalmology, 95:222-228 (1983). For the treatment of glaucoma, a compound of formula (I) may be administered systemically, e.g. by oral or parenteral routes as described below, or topically in the eye in a mineral oil solution or suspension, or
25 aqueous suspension. When used systemically, the compound would be administered in an amount of about 50 to 500 mg per day for an average adult human, while the topical dosage would be about 1 to 3 drops (per eye) of a solution or suspension containing about 1 to 5% by weight of a
30 compound of formula (I) with the dosage being administered about 1 to 4 times per day.

- To prepare the pharmaceutical compositions of this invention, one or more sulfamate compounds of formula (I)
35 are intimately admixed with a pharmaceutical carrier according to conventional pharmaceutical compounding

techniques, which carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral, by suppository, or parenteral. In preparing the compositions in oral dosage form, any of
5 the usual pharmaceutical media may be employed. Thus, for liquid oral preparations, such as, for example, suspensions, elixirs and solutions, suitable carriers and additives include water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the
10 like; for solid oral preparations such as, for example, powders, capsules and tablets, suitable carriers and additives include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like. Because of their ease in administration, tablets
15 and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar coated or enteric coated by standard techniques. Suppositories may be prepared, in which case cocoa butter
20 could be used as the carrier. For parenterals, the carrier will usually comprise sterile water, though other ingredients, for example, for purposes such as aiding solubility or for preservation, may be included. Injectable suspensions may also be prepared, in which case
25 appropriate liquid carriers, suspending agents and the like may be employed.

The pharmaceutical compositions herein will contain, per dosage unit, e.g., tablet, capsule, powder, injection,
30 teaspoonful, suppository and the like, from about 10 to about 500 mg of the active ingredient.

The foregoing compositions are particularly suitable for use in the treatment of epilepsy or the symptoms of
35 epilepsy by a method comprising internally administering to a subject suffering from the symptoms of epilepsy

compositions comprising an effective epilepsy inhibiting amount of a compound of formula (I).

Also part of the present invention are intermediates of the formulae RCH_2OSO_2Cl and $RCH_2OSO_2NH_2$.

In the following Examples and throughout the specification the following abbreviations may be used: g (grams); ml (milliliters); min (minutes); hr (hours); mol (moles); cm (centimeters); v/v (volume to volume); mp (melting point); TLC (thin layer chromatography); NMR (nuclear magnetic resonance); IR (infrared); DMF (dimethylformamide); THF (tetrahydrofuran); and C, H, N, etc. (the chemical symbols for the elements).

Example 1

(Tetrahydro-2H-pyran-2-yl)methane sulfonate

To a cold solution ($-5^{\circ}C$) of tetrahydropyran-2-methanol (2.33 g, 0.02 mol) in DMF (40 ml) was added 50% oily sodium hydride (1.17 g, 0.024 mol as NaH). After stirring for 45 min, sulfonyl chloride (3.42 g, 0.03 mol) was added and the stirring continued for an additional 45 min, at $-5^{\circ}C$. The reaction mixture was poured into cold water and extracted with chloroform. The organic layer was dried (Na_2SO_4) and the solvents were removed under vacuum to give a syrup which was dry column chromatographed (eluted with ethyl acetate:hexane, 4:1 v/v) to give pure (tetrahydro-2H-pyran-2-yl) methanesulfonate as a pale yellow syrup, IR: ($CHCl_3$) 1180 cm^{-1} and 1370 cm^{-1} (OSO_2NH_2).

Example 2

(1-methylcyclohexyl)methane sulfamate

- 5 To a cold solution (-4°C) of (1-methylcyclohexyl)methanol (6.2 g, 0.048 mol) in DMF (90 ml) was added 50% oily sodium hydride (2.81 g, 0.059 mol as NaH). After stirring for 1 hr, sulfamoyl chloride (7.82 g, 0.062 mol) was added and the stirring was continued for an additional 30 min at
- 10 -4°C. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na₂SO₄) and the solvents were removed under vacuum to give a syrup which crystallized upon cooling. Recrystallization from chloroform/hexane gave pure (1-methylcyclo-
- 15 hexyl)methane sulfamate, mp 40°-42°C.

Example 3

supplement

2,3:4,5-Bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate

- 20 To a cold solution (-4°C) of 2,3:4,5-di-O-isopropylidene-β-fructopyranose (75 g, 0.29 mol) in DMF (725 ml) was added 50% ^{NaH} oily sodium hydride (16.34 g, 0.34 mol as NaH).
- 25 After stirring for 90 min, sulfamoyl chloride (54.9 g, 0.48 mol) was added and the stirring continued for an additional 3.5 hr at that temperature. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na₂SO₄) and the
- 30 solvents removed under vacuum to give a syrup which crystallized immediately. Recrystallization from ethylacetate/hexane gave pure 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate, mp 125°-126°C.

Example 42,3:4,5-Bis-O-(1-methylethylidene)-β-D-fructopyranose
methyl sulfamate

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A solution of sulfonyl chloride (93 ml, 1.15 mol) in methylene chloride (100 ml) was added dropwise to a cold solution (-35°C) of 2,3:4,5-di-O-isopropylidene-β-D-fructopyranose (150 g, 0.58 mol) in methylene chloride (400 ml) and pyridine (150 ml). The reaction mixture was allowed to stir and warm to room temperature (25°C); it was stirred for an additional 2 hr. Solvents were removed under vacuum. The resulting semi-solid was dissolved in anhydrous acetonitrile (35 g, 150 ml) and methyl amine was bubbled in. The reaction mixture was tightly stoppered and solvents removed under vacuum. The resulting syrup was subjected to liquid chromatography (dry column ethyl acetate:hexane, 4:1) yielding a light yellow syrup, 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose methylsulfamate, which was homogeneous by TLC and ¹H NMR.

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Example 5(1,2,3,4-Tetrahydro-2-naphthalenyl)methyl sulfamic acid
ester

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To a cold solution (-5°C) of (1,2,3,4-tetrahydro-2-naphthalenyl)methanol (7.1 g, 0.044 mol) in DMF (80 ml) was added 50% oily sodium hydride (2.56 g, 0.054 mol as NaH). After stirring for 45 min, sulfonyl chloride (6.6 g, 0.057 mol) was added and the stirring continued for an additional 95 min at -5°C. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na₂SO₄) and the solvents removed under vacuum to give a syrup which crystallized immediately. Recrystallization from chloroform/hexane gave pure (1,2,3,4-tetrahydro-2-naphthalenyl)methyl sulfamic acid ester, mp 108-109°C, as a white solid.

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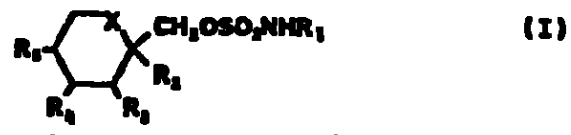
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399

CLAIMS:

1. A sulfamate of the following formula (I):

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wherein

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X is CH₂ or oxygen;

R₁ is hydrogen or alkyl; and

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R₂, R₃, R₄ and R₅ are independently hydrogen or lower alkyl and, when X is CH₂, R₄ and R₅ may be joined to form a benzene ring and, when X is oxygen, R₂ and R₃ and/or R₄ and R₅ together may be a methylenedioxy group of the following formula (II):

20



wherein

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R₄ and R₅ are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

2. The sulfamate of Claim 1, wherein

30

X is oxygen; and

R₂ and R₃ and R₄ and R₅ together are methylenedioxy groups of the formula (II).

3. The sulfamate of Claim 1,
wherein

X is CH₂; and

5

R₄ and R₅ are
ring.

joined to form a benzene

4. The sulfamate of Claim 3,

10

wherein

R₂ and R₃ are hydrogen.

15 5. The sulfamate of Claim 1, wherein said alkyl group for
R₁ is alkyl of about 1 to 4 carbons; said lower alkyl
group for R₂, R₃, R₄ and R₅ is alkyl of about 1 to 3
carbons; and said lower alkyl for R₆ and R₇ is alkyl of
about 1 to 3 carbons.

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6. The sulfamate of Claim 1, wherein said sulfamate of
formula (I) is selected from the group consisting of:

(tetrahydro-2H-pyran-2-yl)methane sulfamate;

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(1-methylcyclohexyl)methane sulfamate;

2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose
sulfamate; *Topiramate*

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2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose
methylsulfamate; or

(1,2,3,4-tetrahydro-2-naphthalenyl)methyl sulfamic acid
35 ester.

7. The sulfamate of Claim 6, wherein said sulfamate is 2,3:4,5-bis-O-(1-methylethylidene)- β -D-fructopyranose sulfamate.
- 5 8. The sulfamate of Claim 6, wherein said sulfamate is (1,2,3,4-tetrahydro-2-naphthalenyl)methyl sulfanic acid ester.
- 10 9. A pharmaceutical composition comprising a sulfamate of ^{preceding claim} any ~~7~~ and a pharmaceutically-acceptable carrier.
10. The pharmaceutical composition of Claim 9, wherein said sulfamate is present in a unit dosage amount of about 10 to 500 milligrams of the sulfamate.
- 15 11. A sulfamate according to any of Claims 1 to 8, or a pharmaceutical composition according to Claim 9 or Claim 10, for use in the treatment of convulsions in a mammal.
- 20 12. A chlorosulfate of the formula RCH_2OSO_2Cl or an azidosulfate of the formula $RCH_2OSO_2N_3$, wherein R is of the following formula (III):

(III)

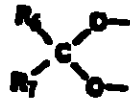
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wherein

- 30 R_2 , R_3 , R_4 and R_5 are independently hydrogen or lower alkyl and, when X is CH_2 , R_4 and R_5 may be alkene groups joined to form a benzene ring and, when X is oxygen, R_2 and R_3 and/or R_4 together may be a methylenedioxy group of the following formula (II):

(II)



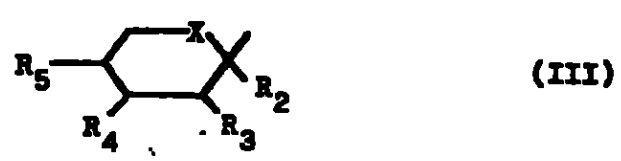
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wherein

R_6 and R_7 are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

13. A method of making a sulfamate according to claim 1, comprising

- (a) reacting an alcohol of the formula RCH_2OH with a chlorosulfamate of the formula $ClSO_2NHR_1$ in the presence of a base, wherein R is a moiety of the formula (III)



and wherein X, R₁, R₂, R₃, R₄ and R₅ are as defined in claim 1, or

- (b) reacting an alcohol of the formula RCH_2OH with sulfonylchloride in the presence of a base, to produce a chlorosulfate of the formula RCH_2OSO_2Cl , wherein R is as defined above, and

- (i) when R₁, in formula (I) is hydrogen or alkyl, reacting said chlorosulfate with an amine of formula R_1NH_2 or
- (ii) when R₁ in formula (I) is hydrogen, reacting said chlorosulfate with a metal azide of formula $RCH_2OSO_2N_3$ and reducing said azidosulfate.

14. A method of making a pharmaceutical composition comprising mixing a sulfamate according to claim 1 with a pharmaceutically-acceptable carrier.

2020
Bogotá, D.C.,

Doctora:
Jimena Escobar Uribe
Apoderada

Oficio N°: 11687

ASUNTO:	Radicación PCT N°	04-117654
	Trámite	011
	Evento	379
	Actuación	440
	Folios	035

Con fundamento en lo previsto por el artículo 43 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica que la oposición presentada por el doctor José Luis Reyes Villamizar, en su calidad de apoderado de Tecnoquímicas S.A., reúne los requisitos formales exigidos por la ley al momento de su presentación.

En cumplimiento de lo dispuesto en la citada norma, se le concede el término de sesenta (60) días hábiles siguientes a la fecha de notificación del presente oficio, para que haga valer sus argumentaciones y presente pruebas.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.


ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha, 13 OCT. 2006.

202021

DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No 04-117654

EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION

PCT FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 562

DE FECHA 31 DE MARZO DEL 2006 EL TERMINO HABIL SEÑALADO POR

LA LEY EXPIRA EL 05 DE JULIO DEL 2006

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI X

NO

Bogotá D.C, ENERO DE 2007

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

304

RADICACIÓN: 4-117884

EDICTO No. 2809

**LA SECRETARÍA GENERAL AD-HOC
HACE SABER:**

Que esta Superintendencia profirió Resolución No. 1165 de 29-ENE-2007. Que el contenido de la parte resolutive es como sigue: El Superintendente de Industria y Comercio.

RESUELVE

ARTICULO PRIMERO: Declarar abandonada la solicitud de privilegio de patente de invención que entró en fase nacional en virtud del Tratado de Cooperación en Materia de Patentes (PCT), de acuerdo con las razones expuestas en la parte considerativa de la presente resolución.

ARTICULO SEGUNDO: Notificar personalmente el contenido de la presente resolución a la

doctora Jimena Escobar Uribe, o a quien haga sus veces, en su calidad de apoderada de Ortho - McNeil Pharmaceutical, Inc., entregándole copia de la misma, advirtiéndole que contra ella procede el recurso de reposición interpuesto ante el Superintendente de Industria y Comercio, al momento de la notificación o dentro de los 5 días hábiles siguientes a ella.

NOTIFÍQUESE Y CUMPLASE

Dada en Bogotá, D.C., a los **29 ENE 2007**

EL SUPERINTENDENTE DE INDUSTRIA Y COMERCIO,


JIMENA ESCOBAR

Para notificar a los interesados, se fija el presente EDICTO en lugar visible al público en la SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO, por el término de (10) diez días hábiles contados a partir de las 8:00 a.m. de hoy.

Secretaría General Ad-Hoc 13-FEB-2007 Este edicto se desflja hoy 28-FEB-2007 a las 4:30 p.m.
Secretaría General Ad-Hoc
EDICTO No. 2809